This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. **(Withdrawn)** A method for identifying genes responsible for high titer antibody production comprising: (a) inactivating mismatch repair of said antibody-producing cells, thereby forming hypermutable cells, (b) screening said hypermutable cells for cells that produce higher titers of antibody as compared to said antibody-producing cells, and (c) analyzing the genomes of said antibody-producing cells and said hypermutable cells, thereby identifying genes responsible for high titer antibody production.

2. **(Withdrawn)** The method of claim 1 wherein said antibody-producing cell produces intact antibodies.

3. **(Withdrawn)** The method of claim 1 wherein said antibody-producing cell comprises endogenous immunoglobulin genes.

4. **(Withdrawn)** The method of claim 1 wherein said antibody-producing cell comprises exogenous immunoglobulin genes.

5. **(Withdrawn)** The method of claim 1 wherein said antibody-producing cell produces derivatives of immunoglobulin genes.

6. **(Withdrawn)** The method of claim 1 wherein said step of in activating mismatch repair comprises introducing into said antibody-producing cells a dominant negative allele of a mismatch repair gene.

7. **(Withdrawn)** The method of claim 1 wherein said step of in activating mismatch repair comprises knocking out at least one mismatch repair gene of said antibody-producing cells.

8. **(Withdrawn)** The method of claim 1 wherein said step of in activating mismatch

repair comprises introducing an RNA interference molecule into said antibody-producing cells.

9. **(Withdrawn)** The method of claim 1 wherein said step of in activating mismatch repair comprises introducing an antisense molecule against a mismatch repair gene into said antibody-producing cells.

10. **(Withdrawn)** The method of claim 6 wherein said allele comprises a truncation mutation.

11. **(Withdrawn)** The method of claim 1 wherein the step of screening comprises analyzing a nucleotide sequence of the genome of said cells as compared to the genome of untreated cells.

12. **(Withdrawn)** The method of claim 1 wherein the step of screening comprises analyzing mRNA expression levels and structure from said cell as compared to untreated cells.

13. **(Withdrawn)** The method of claim 1 wherein the step of testing comprises analyzing protein from the said cell as compared to untreated cells.

14. **(Withdrawn)** The method of claim 1 wherein the step of screening comprises analyzing the phenotype of said gene.

15. **(Withdrawn)** The method of claim 1 wherein said antibody-producing cell is a mismatch repair defective fertilized egg of a non-human animal.

16. **(Withdrawn)** The method of claim 15 further comprising the step of implanting said fertilized egg into a pseudo-pregnant female, whereby said fertilized egg develops into a mature transgenic animal.

17. **(Withdrawn)** A homogeneous culture of high titer antibody producing cells produced by a method comprising the steps of: (a) inactivating mismatch repair of said antibody-producing cells, thereby forming hypermutable cells; (b) screening said hypermutable cells for cells that produce higher titers of antibody as compared to said antibody-producing cells; (c) culturing said hypermutable cells producing higher titers of antibody.

18. **(Withdrawn)** The culture of high titer antibody producing cells of claim 17 wherein the high titer antibody-producing cell is selected from the group consisting of a bacterial cell, a yeast cell, a plant cell, a mammalian cell, a mouse cell, a rat cell, a rabbit cell, a hamster cell, and a non-human primate cell.

19. **(Currently Amended)** A method for producing a high titer antibody producing cell comprising ~~modulating~~ suppressing the expression of ~~at least one gene involved in antibody production~~ alpha-l-anti-trypsin, or endothelial monocyte-activating polypeptide I, or both in an antibody producing cell, such that the cell expresses a higher titer of an antibody as compared with identical cells in which such suppression has not occurred.

20. **(Original)** The method of claim 19 wherein the cell is a hybridoma.

21. **(Withdrawn)** The method of claim 19 where in the cell is an epithelial cell.

22. **(Withdrawn)** The method of claim 19 where in the cell is ovarian.

23. **(Withdrawn)** The method of claim 19 where in the cell is a kidney cell.

24. **(Withdrawn)** The method of claim 19 where in the cell is a myeloid cell.

25. **(Withdrawn)** The method of claim 19 where in the cell is a lymphoid cell.

26. **(Canceled)**

27. **(Withdrawn)** The method of claim 26 wherein the suppressing comprises introducing into the cell an expression vector comprising an antisense transcript to genes encoding endothelial monocyte-activating polypeptide I, alpha-1-anti-trypsin, or both.

28. **(Currently Amended)** The method of claim 19 ~~26~~ wherein the suppressing comprises introducing into the cell a knock out targeting vector to disrupt the function of genes encoding endothelial monocyte-activating polypeptide I, alpha-1-anti-trypsin, or both.

29. **(Withdrawn)** The method of claim 26 wherein the suppressing comprises introducing into the cell a ribozyme to cleave genes encoding endothelial monocyte-activating polypeptide I, alpha-1-anti-trypsin, or both.

30. **(Withdrawn)** The method of claim 26 wherein the suppressing comprises introducing antibodies into the cell, wherein the antibodies specifically bind to the expression product of genes encoding endothelial monocyte-activating polypeptide I, alpha-1-anti-trypsin, or both.

31. **(Withdrawn)** The method of claim 26 wherein the suppressing comprises incubating the cells with a neutralizing antibody or antigen binding fragment thereof, wherein the antibody or antigen binding fragment thereof specifically binds to the expression product of genes encoding endothelial monocyte-activating polypeptide I, alpha-1-antitrypsin, or both that has been secreted into the growth medium of the cells.

32. **(Withdrawn)** A method of modulating antibody production comprising contacting antibody producing cells with at least one protease inhibitor wherein the at least one protease inhibitor decreases antibody production.

33. **(Withdrawn)** The method of claim 32 wherein the at least one protease inhibitor comprises pharmacologically effective amounts of protease substrates.

34. **(Withdrawn)** The method of claim 32 wherein the at least one protease inhibitor is an antibody that specifically binds to endogenous protease inhibitors.

35. **(Withdrawn)** The method of claim 32 wherein the at least one protease inhibitor is an antibody that specifically binds to alpha-1-anti-trypsin.

36. **(Withdrawn)** A method for selecting cells for high titer antibody production whereby growth medium of cells is analyzed for alpha-l-antitrypsin, where low levels are associated with high antibody titers.

37. **(Withdrawn)** The method of claim 36 wherein alpha-1-antitrypsin RNA, wherein low levels of RNA is associated with high antibody titers.

38. **(Withdrawn)** The method of claim 36 wherein alpha-1-antitrypsin protein, wherein low levels of RNA is associated with high antibody titers.

39. **(Withdrawn)** A method for selecting for cells for high titer antibody production whereby growth medium of cells is analyzed for endothelial monocyte-activating polypeptide I, where low levels are associated with high antibody titers.

40. **(Withdrawn)** The method of claim 39 wherein endothelial monocyte-activating polypeptide I RNA, wherein low levels of RNA is associated with high antibody titers.

41. **(Withdrawn)** The method of claim 39 wherein endothelial monocyte-activating polypeptide I protein, wherein low levels of RNA is associated with high antibody titers.

42. **(Withdrawn)** A method for suppressing antibody production in cells associated with hyperimmunoglobulin disease comprising contacting said cells with at least one compound that increases endothelial monocyte-activating polypeptide I gene expression.

43. **(Withdrawn)** A method for suppressing antibody production in cells associated with

hyperimmunoglobulin disease comprising contacting said cells with at least one compound that increases alpha-1-antitrypsin gene expression.

44. **(Canceled)**

45. **(Canceled)**

46. **(Canceled)**

47. **(Withdrawn)** A method for enhancing antibody production associated with hyporimmunoglobulin disease production comprising contacting said cells with at least one compound that suppresses monocyte-activating polypeptide I expression activity.

48. **(Withdrawn)** The method of claim 47 wherein said compound decreases the activity of monocyte-activating polypeptide I protein in said cells.

49. **(Withdrawn)** The method of claim 47 wherein said compound decreases the level of monocyte-activating polypeptide I in said cells.

50. **(Withdrawn)** A host cell for the expression of antibody molecules or fragments thereof comprising a defect in the monocyte-activating polypeptide I gene such that expression of monocyte-activating polypeptide I is inhibited.

51. **(Withdrawn)** The host cell of claim 50 wherein said defect comprises a deletion of the monocyte-activating polypeptide I.

52. **(Withdrawn)** The host cell of claim 50 wherein said defect is a frameshift mutation in the monocyte-activating polypeptide I gene.

53. **(Withdrawn)** The host cell of claim 50 wherein said host cell comprises an expression vector comprising an antisense transcript of the monocyte-activating polypeptide I

gene whereby expression of said antisense transcript suppresses the expression of the monocyte-activating polypeptide I gene.

54. **(Withdrawn)** The host cell of claim 50 wherein said host cell comprises a ribozyme that disrupts expression of the monocyte-activating polypeptide I gene.

55. **(Withdrawn)** The host cell of claim 50 wherein said host cell comprises an intracellular neutralizing antibody against the monocyte-activating polypeptide I protein whereby said antibody suppresses the activity of monocyte-activating polypeptide I.

56. **(Withdrawn)** A host cell for the expression of antibody molecules or fragments thereof comprising a defect in the alpha-l-antitrypsin gene such that expression of alpha-1-antitrypsin is inhibited.

57. **(Withdrawn)** The host cell of claim 56 wherein said defect comprises a deletion of the alpha-1-antitrypsin.

58. **(Withdrawn)** The host cell of claim 56 wherein said defect is a frameshift mutation in the alpha-1-antitrypsin gene.

59. **(Withdrawn)** The host cell of claim 56 wherein said host cell comprises an expression vector comprising an antisense transcript of the alpha-1-antitrypsin gene whereby expression of said antisense transcript suppresses the expression of the alpha-1-antitrypsin gene.

60. **(Withdrawn)** The host cell of claim 56 wherein said host cell comprises a ribozyme that disrupts expression of the alpha-1-antitrypsin gene.

61. **(Withdrawn)** The host cell of claim 56 wherein said host cell comprises an intracellular neutralizing antibody against the alpha-1-antitrypsin protein whereby said antibody suppresses the activity of alpha-1-antitrypsin.

62. **(Withdrawn)** The host cell of claim 61 further comprising an expression vector comprising a polynucleotide sequence encoding at least a portion of an antibody molecule.

63. **(Withdrawn)** The host cell of claim 61 wherein said polynucleotide encodes at least an immunoglobulin light chain or fragment thereof.

64. **(Withdrawn)** The host cell of claim 61 wherein said polynucleotide encodes at least an immunoglobulin heavy chain or fragment thereof.

65. **(Withdrawn)** The method of claim 1 further comprising the step of restabilizing the genome of selected high titer antibody-producing cells.

66. **(Withdrawn)** A culture of stable, high titer antibody-producing cells made by the method of claim 65.

67. **(Canceled)**

68. **(Withdrawn)** The method of claim 26, wherein the suppressing comprises introducing into the cell an oligonucleotide antisense to the gene encoding alpha-1-antitrypsin, endothelial monocyte activating polypeptide I, or both.

69. **(Withdrawn)** A method for enhancing antibody production in cells associated with hypoimmunoglobulin disease comprising contacting the cells with at least one compound that suppresses monocyte-activating polypeptide I activity.

70. **(Withdrawn)** A method for enhancing antibody production in cells associated with hypoimmunoglobulin disease comprising contacting the cells with at least one compound that decreases the level of expressed alpha-1-antitryspin in the cells.

71. **(Withdrawn)** The method of claim 32, wherein the antibody producing cells are hybridomas, epithelial cells, ovarian cells, kidney cells, myeloid cells, or lymphoid cells.

72. **(New)** The method of claim 19, wherein the cell is a rodent cell.